ecules are primarily separated by different electrophoretic mobilities caused by their different molecular size, shape and/or charge. Microcapillary tubes have recently been used for use in microcapillary gel electrophoresis (high performance capillary electrophoresis (HPCE)). One advantage of HPCE is that the heat resulting from the applied electric field is efficiently dissipated due to the high surface area, thus allowing fast separation. The electrophoresis module serves to separate sample components by the application of an electric field, with the movement of the sample components being due either to their charge or, depending on the surface chemistry of the microchannel, bulk fluid flow as a result of electroosmotic flow (EOF).

[0135] As will be appreciated by those in the art, the electrophoresis module can take on a variety of forms, and generally comprises an electrophoretic microchannel and associated electrodes to apply an electric field to the electrophoretic microchannel. Waste fluid outlets and fluid reservoirs are present as required.

[0136] The electrodes comprise pairs of electrodes, either a single pair, or, as described in U.S. Pat. Nos. 5,126,022 and 5,750,015, a plurality of pairs. Single pairs generally have one electrode at each end of the electrophoretic pathway. Multiple electrode pairs may be used to precisely control the movement of sample components, such that the sample components may be continuously subjected to a plurality of electric fields either simultaneously or sequentially.

[0137] In a preferred embodiment, electrophoretic gel media may also be used. By varying the pore size of the media, employing two or more gel media of different porosity, and/or providing a pore size gradient, separation of sample components can be maximized. Gel media for separation based on size are known, and include, but are not limited to, polyacrylamide and agarose. One preferred electrophoretic separation matrix is described in U.S. Pat. No. 5,135,627, hereby incorporated by reference, that describes the use of "mosaic matrix", formed by polymerizing a dispersion of microdomains ("dispersoids") and a polymeric matrix. This allows enhanced separation of target analytes, particularly nucleic acids. Similarly, U.S. Pat. No. 5,569,364, hereby incorporated by reference, describes separation media for electrophoresis comprising submicron to above-micron sized cross-linked gel particles that find use in microfluidic systems. U.S. Pat. No. 5,631,337, hereby incorporated by reference, describes the use of thermoreversible hydrogels comprising polyacrylamide backbones with N-substituents that serve to provide hydrogen bonding groups for improved electrophoretic separation. See also U.S. Pat. Nos. 5,061,336 and 5,071,531, directed to methods of casting gels in capillary tubes.

[0138] In a preferred embodiment, the devices of the invention include a reaction module. This can include either physical, chemical or biological alteration of one or more sample components. Alternatively, it may include a reaction module wherein the target analyte alters a second moiety that can then be detected; for example, if the target analyte is an enzyme, the reaction chamber may comprise an enzyme substrate that upon modification by the target analyte, can then be detected. In this embodiment, the reaction module may contain the necessary reagents, or they may be stored in a storage module and pumped as outlined herein to the reaction module as needed.

[0139] In a preferred embodiment, the reaction module includes a chamber for the chemical modification of all or part of the sample. For example, chemical cleavage of sample components (CNBr cleavage of proteins, etc.) or chemical cross-linking can be done. PCT US97/07880, hereby incorporated by reference, lists a large number of possible chemical reactions that can be done in the devices of the invention, including amide formation, acylation, alkylation, reductive amination, Mitsunobu, Diels Alder and Mannich reactions, Suzuki and Stille coupling, chemical labeling, etc. Similarly, U.S. Pat. Nos. 5,616,464 and 5,767,259 describe a variation of LCR that utilizes a "chemical ligation" of sorts. In this embodiment, similar to LCR, a pair of primers are utilized, wherein the first primer is substantially complementary to a first domain of the target and the second primer is substantially complementary to an adjacent second domain of the target (although, as for LCR, if a "gap" exists, a polymerase and dNTPs may be added to "fill in" the gap). Each primer has a portion that acts as a "side chain" that does not bind the target sequence and acts as one half of a stem structure that interacts non-covalently through hydrogen bonding, salt bridges, van der Waal's forces, etc. Preferred embodiments utilize substantially complementary nucleic acids as the side chains. Thus, upon hybridization of the primers to the target sequence, the side chains of the primers are brought into spatial proximity, and, if the side chains comprise nucleic acids as well, can also form side chain hybridization complexes. At least one of the side chains of the primers comprises an activatable cross-linking agent, generally covalently attached to the side chain, that upon activation, results in a chemical cross-link or chemical ligation. The activatible group may comprise any moiety that will allow cross-linking of the side chains, and include groups activated chemically, photonically and thermally, with photoactivatable groups being preferred. In some embodiments a single activatable group on one of the side chains is enough to result in cross-linking via interaction to a functional group on the other side chain; in alternate embodiments, activatable groups are required on each side chain. In addition, the reaction chamber may contain chemical moieties for the protection or deprotection of certain functional groups, such as thiols or amines.

[0140] In a preferred embodiment, the reaction module includes a chamber for the biological alteration of all or part of the sample. For example, enzymatic processes including nucleic acid amplification, hydrolysis of sample components or the hydrolysis of substrates by a target enzyme, the addition or removal of detectable labels, the addition or removal of phosphate groups, etc.

[0141] In a preferred embodiment, the target analyte is a nucleic acid and the biological reaction chamber allows amplification of the target nucleic acid. Suitable amplification techniques include, both target amplification and probe amplification, including, but not limited to, polymerase chain reaction (PCR), ligase chain reaction (LCR), strand displacement amplification (SDA), self-sustained sequence replication (3 SR), QB replicase amplification (QBR), repair chain reaction (RCR), cycling probe technology or reaction (CPT or CPR), and nucleic acid sequence based amplification (NASBA). Techniques utilizing these methods and the detection modules of the invention are described in PCT US99/01705, herein incorporated by reference in its entirety. In this embodiment, the reaction reagents generally com-